

thorax is due to the rupture of emphysematous vesicles. If this were true the condition would be expected to affect the two sides impartially.

One case only, the one which terminated fatally, presented undeniable signs of infection with tubercle. Another had a family history of tuberculosis, and had had bronchitis and pleurisy in the interval between two manifestations of pneumothorax. A third case gave a history of cough and bloody expectoration preceding her first pneumothorax. One case showed Roentgen-ray findings pointing to tubercle infection. In the remaining two cases there was no apparent valid reason for suspecting the presence of a latent tuberculosis.

Conclusions regarding the etiology of recurrent pneumothorax would be out of place with so little data at hand. It is reasonable to suppose that it is the same as in cases of "spontaneous" pneumothorax. The etiology of this condition has been quite thoroughly discussed, West²⁰ making the point that tuberculosis is always the causative factor. This series of cases, with four showing definite or suggestive signs of tubercle infection, is not without interest.

A CLASSIFICATION AND ANALYSIS OF CLINICAL TYPES OF SPLENOMEGALY ACCOMPANIED BY ANEMIA.¹

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CHRONIC splenomegaly, usually associated with anemia, is not an uncommon condition both in adults and children. The forms without leukocytosis, more or less related to "splenic anemia," it is my intention to consider here, omitting the types of enlarged spleen in which other features render differentiation easy (such as leukemia, pseudoleukemia, polycythemia, and those secondary to obstruction or infection, as in heart disease, typhoid, kala-azar, syphilis, and so forth).

SPLenic ANEMIA. The connection between chronic enlargement of the spleen and marked anemia without leukocytosis, as denoted in the term "splenic anemia," was first established forty-eight years ago by Gretzel,² in Griesinger's clinic, in Berlin. He described the

²⁰ Samuel West, *Pneumothorax*, *Lancet*, 1897, i, 1264.

¹ Being part of an address read before the Joint Meeting of the Pediatric Societies, New York Academy of Medicine, November 5, 1914.

² Ein Fall von Anemia Splenica bei Einem Kind, *Berl. klin. Woch.*, 1866, ii, 212.

case of a child, ten months old, suffering from dysentery and severe anemia, with considerable enlargement of the spleen and lesser enlargement of the liver and lymph nodes. Examination of the blood showed that the proportion of white to red cells was not increased—that is, that it was not leukemia. Five years later H. C. Wood³ described a “splenic variety” of pseudoleukemia, with a report of a case with a greatly enlarged spleen, severe anemia, and without leukocytosis. It must be remembered that at this time not only was pathological anatomy in its infancy, but also no exact methods existed for examining the condition of the blood. A term, therefore, like “splenic anemia,” which a half century ago was a distinct advance in differentiating a new type of disease, but which now is known to include several distinct types, should now either be properly restricted or discarded entirely. By restriction I mean limitation of the term to the earlier or precirrhotic stages of Banti’s disease, with which it is apparently identical. The fact that in most cases the etiology or pathogenesis of this group of diseases is not yet clearly understood is no more an argument for continuing to group them under such loose terms as “splenic anemia” or “splenomegaly with anemia” than it would have been to group typhoid with typhus fever until the discovery of the *Bacillus typhosus*. Though much still remains to be learned in regard to them, and though probably even their present eponymic or cumbersome names are only temporary, nevertheless it has already become more profitable to deal with them as independent affections. The inconvenience resulting from the present use of the term “splenic anemia” is quickly demonstrated to anyone making a critical survey of the literature. Statistical summaries, including valuable detailed information, are thus frequently rendered useless when, on analysis, they are found to include several independent types.

Recently evidence has been put forth to show that these conditions are perhaps related to other commoner diseases, such as pernicious anemia, various hemolytic anemias (*Dibothriocephalus latus* and *uncinariasis*), thrombosis of the portal vein or artery, and some splenic types of cirrhosis of the liver. It will be beyond my scope to more than indicate such relations. The better differentiated of these offsprings of splenic anemia are Banti’s disease, Gaucher’s disease (or large-celled splenomegaly), v. Jaksch’s pseudoleukemia infantum, the Hayem-Widal or acquired form of hemolytic jaundice with splenomegaly, and the Chauffard-Minkowski or congenital or hereditary form of the same. I have indicated some of the differential points of these diseases in the following table:

³ On the Relation of Leukocythemia and Pseudoleukemia, *AMER. JOUR. MED. SCI.*, 1871, lxii, 373.

TABLE I.—DIFFERENTIAL DIAGNOSIS.

	Etiology.	Pathology of spleen.	Family history.	Time of onset.	Duration.	Icterus.	Splenomegaly.	Hemorrhages.	Anemia	Resistance of red blood cells.	Reticulated red blood cells.	Urobilinuria.	Leukocytes in blood.	Liver.	Treatment.
Gaucher's disease	Toxin ? Infection ? Tumor ?	Peculiar cell hyperplasia	Occasionally positive	Childhood	Many years	Rare	+++	Occasionally	Slight	?	?	?	—	+	Splenectomy ?
Banti's disease	Toxin ? Infection ?	Hypertrophy fibrosis	Negative	Adult life	Few years	Rare	+	Occasionally	Slight to severe	Normal	Normal	+	—	First + Later —	Splenectomy.
v. Jaksch's disease	Rachitis ?	Hypertrophy fibrosis	Negative	Infancy	Several months	Rare	++	?	Slight to severe	?	?	?	+	+	Splenectomy ? Iron, arsenic, etc.
Hayem-Widal	1. Primary ? 2. Secondary to infection	Congestion and pigmentation	Negative	Any age	Many years	Present	++	Rare	Severe	Diminished	Increased	+	—	+ or normal	Splenectomy.
Chauffard-Minkowski	Heredity	Congestion and pigmentation	Positive	Congenital or childhood	Many years	Present	++	0	Slight	Diminished	Increased	+	—	+	Splenectomy.
Pernicious anemia	Enterogenous toxin ?	Fibrosis	Negative	Adult life	Few years with remissions	Very rare	Slight or diminished	Rare	Severe	Increased	Increased	+	— or +	Normal	Iron, arsenic, etc. (splenectomy questionable).

GAUCHER'S DISEASE. Gaucher's disease, or large-celled splenomegaly, was probably the first variety to be differentiated on account of its peculiar anatomical picture. Although in reality possessing little in common with the other forms of splenic anemia, I will consider it in some detail on account of the similarity of the clinical picture and from the fact that it is still included by many writers under this heading. First described by Gaucher,⁴ in 1882, as a primitive epithelioma it was later shown not to possess the characters of malignancy. Bovaird⁵ called it a simple hyperplasia and Brill and Mandlebaum⁶ showed that it arose simultaneously from the endothelium of the spleen, lymph nodes, and bone-marrow. The characteristic large vesicular cells, with small eccentric nuclei, blocking the sinuses of the spleen and lymph nodes or crowded in the capsules of the liver lobules should make the diagnosis easy at autopsy. Careful analysis by the last-named authors, however, with rejection of falsely diagnosed cases, has reduced the number of reported cases to fourteen. Since that time five apparently true cases have been reported by Knox and Wahl⁷ and Hermann.⁸ Brill and Mandlebaum's excellent summary reveals the following clinical picture: The disease begins insidiously in infancy or childhood (usually before the thirteenth year) and pursues a chronic course (average of twenty years). As in some of the other varieties a history of similar trouble in the family is frequently elicited. No great disturbance in the health of the individual occurs until the disease has persisted for some time, when distinct anemia appears and, as in Banti's disease, a definite tendency to submucous or subcuticular hemorrhages. These, however, are never fatal, and death usually occurs from an intercurrent affection. The most prominent symptom is the progressive enlargement of the spleen, which may reach greater proportions than in any other disease, eventually filling most of the abdomen. The abdominal discomfort produced by the enlarged spleen may be the first indication of the disease. As in Banti's disease the blood changes are not very characteristic. The anemia of chlorotic type is never very severe (average red blood corpuscles count of advanced cases being 3,700,000). A definite leukopenia is usually found, though the differential count remains unchanged. No enlargement of the superficial lymph nodes can be found, and jaundice and ascites are rarely present. Liver enlargement, succeeding that of the spleen, may eventually reach considerable proportions.

⁴ De l'Epithelioma Primitif de la Rate, Thèse de Paris, 1882.

⁵ Primary Splenomegaly, Endothelial Hyperplasia of the Spleen, AMER. JOUR. MED. SCI., 1900, cxx, 377.

⁶ Large-cell Splenomegaly (Gaucher's Disease), AMER. JOUR. MED. SCI., 1913, cxlvi, 863.

⁷ A Case of Primary Splenomegaly of the Gaucher Type, Med. Rec., 1914, lxxxvi, 606.

⁸ A Case of Gaucher's Disease, Med. Rec., 1914, lxxxvi, 606.

A brownish discoloration of the skin has been noticed with a "peculiar yellowish wedge-shaped thickening of the conjunctivæ, commonly seen on both sides of the corneæ." In spite of the rather negative character of the symptoms the disease has been recognized three times during life, with confirmation of the diagnosis by histological examination.⁹

Its etiology is still in doubt. Malignancy having been discarded, various theories of endogenous toxins, splenic enzymes, or of infection have been offered, but supported by very little evidence.

In regard to the bearing of experimental spleen work on this disease, but few facts exist to help us. Splenectomy has been tried in nine cases, with three deaths. This probably represents too high a mortality, but, on the other hand, a cure could hardly be expected, as the disease is known to exist independently in bone marrow and lymph nodes. The resistance of the red cells and number of skinned cells (as evidence of blood regeneration), as far as I can find, has not been studied, but in view of the absence of signs of increased hemolysis, one would not expect to find any noteworthy changes in such examinations. The red bone marrow, usually found at autopsy, on the other hand, would point to efforts at regeneration. As the splenic tissue is largely replaced by the peculiar Gaucher type of cell, it may be that this stimulated marrow is equivalent to that found experimentally after splenectomy.

Summing up: this disease, in spite of being frequently included among other forms of splenic anemia, has but little in common with them clinically, beyond the chronically enlarged spleen and anemia. Pathological examination should always admit its proper diagnosis to be made.

In the past few months, under the title of "an unknown disease picture," Niemann¹⁰ has described a form much resembling Gaucher's disease, but running an acute course, with fatal termination after fifteen months. The finding of similar large endothelial-like cells at autopsy make it probable that an acute form of this disease must also be recognized.

BANTI'S DISEASE. For the more common condition of Banti's disease, or splenomegaly with hepatic cirrhosis, a brief summary will suffice to recall its general symptomatology. First described by Guido Banti¹¹ in 1894 the clinical picture presented at that time still holds. Usually occurring in young otherwise healthy adults, and running a chronic course, its symptomatology may be divided into three periods: in the first or pre-ascitic period, usually lasting

⁹ While this paper was in press, Bernstein has reported (*Jour. Am. Med. Assoc.*, 1915, lxiv, 1907) a fourth case diagnosed by clinical symptoms, and confirmed before operation by splenic puncture.

¹⁰ Ein unbekanntes Krankheitsbild, *Jahrb. f. Kinderheilk.*, 1914, lxxix, 1.

¹¹ La Splenomegalia con Cirrosi Epatica, *Lo Sperimentale*, 1894, Sez. Biol., xlviii, 407.

several years, a gradually increasing weakness and pallor are noticed with digestive disturbances and abdominal pain, which may first call attention to the enlarged, smooth, hard spleen. A tendency to hemorrhages with a moderate anemia of chlorotic type is usually present, but may be postponed until the later stages. There is nothing specially characteristic in the anemia, the increase of urobilin being the only sign of increased blood destruction. The resistance of the red cells is unchanged; signs of a regenerating bone marrow (nucleated and reticulated red cells) are slight or absent. After splenectomy, however, such changes may be noted. In such a case that I have recently had occasion to examine the red cells showed the most marked increase in resistance that I have seen clinically (complete hemolysis did not occur even at 0.25 per cent. NaCl). Though no nucleated reds were present in the circulation, reticulated forms were more numerous than before splenectomy. A slight leukopenia is characteristic. The second, or intermediate, stage lasts but a few months, is characterized by scanty, high-colored urine, containing an excess of urobilin; and by attacks of dyspepsia and diarrhea, with slight increase in the size of the liver. The third stage is ushered in by the symptoms of cirrhosis, a recurrent, painless ascites, occasionally slight jaundice, shrunken liver, and increasing anemia and emaciation. After a few years an intercurrent infection or fatal hemorrhage terminates the scene. The first two of these periods are identical with the "splenic anemia" of adults. It is hardly necessary to say that such a picture is subject to variation, and that in some cases these three periods cannot be distinguished.

In spite of the great amount of work done on Banti's disease in the past twenty years its pathogenesis is still undetermined. Except for a recent statement by Gibson¹² that he had found streptothrix in certain cases of enlarged spleen resembling Banti's disease, its etiology is still unknown. Yates, Bunting, and Kristjanson¹³ have found diphtheroid organisms in several cases of Banti's disease, and consider the condition closely related to that of Hodgkin's disease. An apparently identical syndrome can be brought about by thrombosis of the portal or splenic vein (Edens,¹⁴ Goldmann¹⁵), and similar clinical pictures have followed various infections, local trauma, etc. Hollins¹⁶ has recently produced a similar condition in rabbits with injections of *Bacillus coli*. Banti, who first considered the enlarge-

¹² On Certain Causes of Splenomegaly and Banti's Disease, *Proc. Roy. Soc.*, 1914, vii, Med. Sect., 7.

¹³ The Etiology of Splenic Anemia or Banti's Disease, *Jour. Amer. Med. Assoc.*, 1914, lxiii, 2225.

¹⁴ Ueber Milzvenenthrombose, Pfortaderthrombose und Bantische Krankheit, *Mitth. a. d. Grenz. d. Med. u. Chir.*, 1907, xvii, 59.

¹⁵ Zur Kasuistik der Milzvenen u. Pfortaderthrombose, *Deut. med. Woch.*, 1913, xxxix, 1542.

¹⁶ Primary Splenomegaly or Splenic Anemia, *Practitioner*, 1915, xciv, 426.

ment of the spleen to be primary, later stated that the infectious agent was brought by the artery either as a direct toxin or as a substance which, from the pathological splenic metabolism, was changed into a splenotoxin. The theory has never been confirmed by facts. The unquestioned improvement, however, that results in many cases after splenectomy, proves that the altered spleen is at least an important pathogenetic factor. This is still further emphasized by Umber's¹⁷ interesting observation: during splenectomy for Banti's disease in a boy, aged fifteen years, a small piece of the enlarged liver was excised for histological examination and a distinct peripheral infiltration found. After the operation the liver quickly returned to normal size, a strong indication of the splenogenous origin of the hepatitis which, if undisturbed, would have progressed to the usual cirrhosis. In metabolic experiments on this patient, Umber found a nitrogen deficit that was changed to a nitrogen balance by splenectomy. This, however, has not been confirmed by later authorities.

In the pathology of the disease there is nothing specially distinctive. The enlarged spleen usually shows an increased amount of fibrous tissue in the capsule and reticulum known as "fibro-adenie" (that is, increased fibrous tissue, but retaining an adenoid appearance), and involving both pulp and follicles. The Malpighian follicles, especially in the later stages, are small and scarce; in the earlier stages they may be hyperplastic and the "fibro-adenie" be absent. Macrophages, increased amount of pigment, and other evidences of increased blood destruction are usually found. The changes in the liver are those of an ordinary periportal cirrhosis.

In summarizing, one might say that although the etiology of Banti's disease is unknown, and may well be from several sources, evidence points to the close causative relationship of the spleen. One would not expect the removal of the largely fibrotic organ of the later stages to be attended with marked somatic changes, and it is precisely in the earlier stages of the disease in which splenectomy has proved most beneficial.

VON JAKSCH'S DISEASE. The anemia infantum pseudoleukemica of von Jaksch is in all probability not an independent condition, but represents an atypical response of the infantile hemopoietic system to one of the primary diseases of the blood (leukemia, pernicious anemia, the secondary anemia of rickets, syphilis, or the formerly unrecognized types of hemolytic jaundice). A high-grade anemia, with blood picture somewhat resembling pernicious anemia, appears in infants of one or two years. The smooth, hard spleen is conspicuously large, while the liver, in contrast to the liver of leukemia in childhood, is slightly enlarged. Benjamin has lately found rickets present in

¹⁷ Zur Pathologie der Bantischen Milz Krankheit, Münch. med. Woch., 1912, lix, 1473.

all of a series of such cases examined by him, and suggests the name "Rachitische Megalosplenie." That von Jaksch's disease is being less and less regarded as a separate disease is shown by its gradual disappearance from the text-books.

HEMOLYTIC JAUNDICE. The acquired and congenital or familial types of hemolytic jaundice with splenomegaly (Hayem-Widal and Chauffard-Minkowski) are frequently grouped by English and American authors under such titles as hemolytic jaundice (Thayer),¹⁸ chronic family jaundice (Tileston).¹⁹ As the two forms possess several rather important and characteristic differences, however, I have deemed it advisable to follow the continental custom and consider them as independent conditions. Search for their true etiology and pathogenesis is more apt to be stimulated under such an arrangement than if they are grouped together. Furthermore, Widal, Abrami and Brulé,²⁰ experimenting with toluylendiamin, have offered evidence that the two types are of different origin.

They have been so recently differentiated that they can be best considered together in their historical development. Although Murchison,²¹ Wilson,²² and others had previously described cases of chronic jaundice occurring in several members of a family (in Murchison's case splenomegaly is not mentioned), a more complete description by Hayem,²³ in 1898, was the first to establish an independent clinical condition. The clinical picture of the five cases analyzed by him was as follows: All five exhibited a chronic jaundice, with the presence of bile pigment in the blood serum, but not in the urine (*i. e.*, acholuric icterus). The other signs of obstructive jaundice, such as itching, bradycardia, and clay-colored stools, were also lacking. A distinct anemia, the red-cell count varying from 1,000,000 to 3,000,000, was present in all. Very large, hard spleens were found in each case and slight enlargement of the liver was also noted. Exacerbations were frequent, in which the jaundice deepened and bile appeared in the urine. The importance of these exacerbations was emphasized by Widal, who termed them "crises of deglobulization," and considered them highly characteristic of the acquired form. In severe cases the blood count may drop below 1,000,000, and hemoglobin appear in the urine. In all five of Hayem's cases the family history was negative, and in three the jaundice was stated to have appeared first in adult life.

¹⁸ Hemolytic Jaundice, Illinois Med. Jour., 1911, xix, 174.

¹⁹ Chronic Family Jaundice, AMER. JOUR. MED. SCI., 1910, cxxxix, 847.

²⁰ Pluralité d'Origine des Ictères Hemolytiques, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1354.

²¹ Case of Hereditary Jaundice and Gout, "Diseases of Liver," 1885, p. 481 (3d ed.).

²² Some Cases Showing Hereditary Enlargement of the Spleen, Trans. Clin. Soc., London, 1890, xxiii, 162; *ibid.*, 1893, xxvi, 163.

²³ Sur un Variété Particulière d'Ictère Chronique, Ictère Infectieux Chronique Splénomégalique, Presse Méd., 1898, i, 121; Nouvelle Contribution à l'Etude de l'Ictère Infectieux Chronique Splénomégalique, Bull. et Mém. Soc. Méd. des Hôp. de Paris, 1908, xxv, 122.

Two years later Minkowski²⁴ described a similar disease occurring in eight members of one family in three generations. This has subsequently proved to be commoner than the acquired form. In addition to the symptoms of Hayem's cases an increased amount of urobilin was noted in the urine. Autopsy revealed no cirrhosis of the liver or obstruction of the bile passages. The spleen showed a diffuse hyperplasia and hyperemia. Pigment deposits were numerous in the kidneys and centres of the liver lobules.

The next important contribution to the clinical picture of these diseases was made by Chauffard,²⁵ who showed in the congenital type that the resistance of the red-blood cells to hypotonic salt solution was much diminished. This simple test, suggested in 1903 by Ribierre,²⁶ has proved so useful in our experimental work that I take the liberty of describing it briefly:

A series of twelve or more tubes containing 1 c.c. of different strengths of hypotonic salt solution are arranged varying from 0.25 per cent. to 0.6 per cent. (or even stronger if diminished resistance is suspected). Into each one drop of whole blood is introduced and the tube gently shaken. If the drops have been of different size, occasionally slightly more blood may be added until the color is the same in all. After standing two hours at room temperature, in the stronger solutions in which no hemolysis has occurred, the unchanged corpuscles at the bottom of the tube will be overlaid with colorless salt solution. In the weakest solutions all corpuscles will have been hemolyzed, forming a transparent red solution. In the intermediate tubes can be noted at which strength hemolysis begins and at which it is complete. In normal cases, hemolysis begins at about 0.45 per cent. and is complete at 0.35 per cent. In a case of the familial type that I recently had occasion to examine, hemolysis began as high as 0.7 per cent. and was already complete at 0.475 per cent. Widal, Abrami and Brulé showed that in some cases of the acquired form, with apparently normal resistance, fragility could be demonstrated if the cells were washed free of plasma. Later work, however, has shown that any change, when present, is in the cells themselves.

Increased number of microcytes and of reticulated red cells by methods of vital staining were found by Chauffard²⁷ in the congenital, or familial type, and their presence later confirmed also in the acquired type. In the case above mentioned I found about 5 per cent. of the red cells reticulated as opposed to the normal of

²⁴ Ueber einem Hereditärischen unter dem Bild eines Chronischen Ikterus mit Urobilinurie, Splenomegalie und Nieren Siderosis verlaufende Affektion, Verh. der Deut. Kong. f. inn. Med., 1900, xviii, 316.

²⁵ Pathogenie de l'Ictère Congénitale de l'adult, Semaine Méd., 1907, xxvii, 25; Les Ictères Hemolytiques, Semaine Méd., 1908, xxviii, 49; Pathogenie de l'Ictère Hemolytique Congénitale, Annales de Méd., 1914, i, 1.

²⁶ L'Hémolyse et la Mesure de la Resistance Globulaire, Thèse de Paris, 1903.

²⁷ Loc. cit.

less than 1 per cent. In some cases the figures have run as high as 20 per cent. Although Chauffard used pyroninmethyl green stain and Widal, polychrome methylene blue, we have obtained the best results with brilliant cresyl blue. A few drops of blood are dropped into a small test-tube containing a weak solution of the stain, with a little potassium oxalate to prevent rouleaux formation. After standing ten to fifteen minutes some of the sediment is pipetted off and a fresh cover-slip preparation made. The percentage of the reticulated to the non-reticulated forms is then estimated under oil immersion. If the reticulated cells are increased it is generally considered evidence of more active blood formation.

Another diagnostic method, the auto-agglutination test, is advocated by Widal, Abrami and Brulé.²⁸ This test consists merely of mixing one drop of the patient's washed red blood cells with ten drops of his own serum in a watch-glass. If positive, after some seconds, the mixture loses its homogeneous aspect, forms visible granules of agglomerated corpuscles on agitating, and finally, after several minutes, forms a distinct pellicle that sinks to the bottom and does not mix with the clear serum on shaking. They have found it always positive in the acquired form and always negative in the congenital or familial type. In the case I have previously mentioned this test proved negative. However, in Micheli's²⁹ carefully studied case of the acquired type this test was also negative. Isohemolysins have occasionally been found in both types (Micheli,³⁰ Hopkins³¹) but are not supposed to possess any pathological significance. Although both types of hemolytic jaundice usually run a chronic course, Gaisböck³² has shown that an acute malignant form may occur that is fatal in a few months.

Therefore, the cardinal symptoms of these types of hemolytic jaundice with splenomegaly are found to be a chronic enlargement of the spleen, existing with an acholuric, non-obstructive jaundice, and anemia, frequently paroxysmal in character and varying in intensity. Increased blood destruction is indicated by increased urobilin in the urine, and various characteristic changes are found in the blood. The red cells show diminished resistance to hypotonic salt solution, increased number of reticulated cells with vital staining, and in the acquired form the phenomenon of auto-agglutination of the red corpuscles. The blood serum rarely contains auto- or isohemolysins.

²⁸ Auto-agglutination des Hematies, dans l'Ictère Hemolytique Acquis, *Comp. Rendu. Soc. de Biol.*, 1908, lxiv, 655; Les Ictères d'Origine Hemolytique, *Arch. des Mal. de Cœur*, 1908, i, 193.

²⁹ Unmittelbare Effekte der Splenektomie bei einer Fall von Erworbenem Hemolytischen Splenomegalischen Icterus, *Wien. klin. Woch.*, 1911, xxiv, 1269.

³⁰ *Loc. cit.*

³¹ Two Instances of Chronic Family Jaundice, *AMER. JOUR. MED. SCI.*, 1913, cxlvi, 726.

³² Beiträge zur Klinik hemolytischer Anämien mit herabgesetzter osmotischer Erythrocyten Resistenz, *Deut. Arch. f. klin. Med.*, 1913, cx, 413.

I have purposely postponed until now a consideration of the differentiation of the acquired and familial types and their relation to other conditions, such as those suggested by Gilbert³³ and Banti.³⁴ The fact that in the acquired group the disease is definitely acquired in adult life, whereas in the other there is a family history of the same trouble would not in itself be sufficient to warrant the formation of independent disease pictures. There are, however, other features which tend to differentiate their appearance more strongly. In the congenital form the subjects, as Chauffard puts it, "are more icteric than sick." Frequently they come for treatment for other conditions and consider the chronic jaundice as a family idiosyncrasy not interfering with perfect health. The acquired form, on the other hand, is usually ushered in with a definite attack of illness, the anemia becomes much more grave, sometimes as low as 1,000,000, and the patient is distinctly more anemic than jaundiced. In De Castello's³⁵ case, that showed great improvement after splenectomy, the red-cell count had previously fallen to 800,000.

In an analysis of 158 cases of hemolytic jaundice in which blood counts were available, I found 55 belonging to the acquired type and 103 to the congenital or familial type. Of these 103 only 23 failed to give a positive family history, whereas of the 80 familial cases 35 developed after birth. The average red-cell count of the 55 acquired cases was 2,032,000, the counts ranging from 510,000 to 4,500,000. (Counts below 1,000,000 were recorded in 10 cases, below 2,000,000 in 27 cases, and over 4,000,000 in only 4 cases.) The average count of the 103, congenital and familial, was 3,340,000, the counts ranging from 1,800,000 to 5,700,000. (N. B.—One familial case reported by v. Krannhals³⁶ showed 1,000,000 red cells in a single count, but as the hemoglobin was between 55 and 65 per cent. the accuracy of the count is questionable. No counts were recorded below 1,000,000, 8 below 2,000,000, and 25 above 4,000,000. The average of the familial cases was 3,281,000; of the congenital, 3,543,000.) These figures show that there is a much more marked anemia in the cases of the acquired type than in the familial.

Widal and his pupils claim that the auto-agglutination test is only positive in the acquired form, and considers it important evidence that the two diseases have fundamentally different origins. I have already called attention to the differential importance of

³³ Cholémié Familiale, Bull. Mém. Soc. Méd. des Hôp. de Paris, 1907, xxiv, 1203. (N. B.—This contains references to all of Gilbert's work on this subject to date.)

³⁴ La Splenomegalia Emolitica, Patologica, 1911, iii, 471; La Splenomegalia Emolitica Anemopoietica, Sperimentale, 1913, lxvii, 323.

³⁵ Discussion of Kahn's case, Verhand. d. deut. Kong. f. inn. Med. (Wiesbaden), 1913, xxx, 331.

³⁶ Ueber Congenitale Ikterus mit Kronischem Milztumor, Deut. Arch. f. klin. Med., 1904, lxxxi, 596.

Widal's "crises of deglobulization," although it must be admitted that marked fluctuations are present also in the familial type.

Cases have been reported where a condition apparently identical with the acquired form under discussion has followed attacks of malaria, syphilis, and other infections, and further study will probably reveal that all cases of this type are due to more or less obscure intoxication. The signs of excessive blood destruction usually disappear from these cases when the underlying cause is successfully treated. The familial form, on the other hand, appears more as an inherited dystrophy of the hemopoietic system, rendering the red-blood cells more easily destructible. On this basis Chauffard at first strongly advised against splenectomy in this type, but subsequent cases have shown such improvement after this treatment that it would seem as if the removal of this site of blood destruction was advisable, whether or not it is the primary seat of the trouble. After Kahn's³⁷ and Roth's³⁸ successful splenectomies of the familial type the resistance of the red cells failed to return to normal.

The congenital type, with negative family history, grouped with the familial type by most authors, has less grounds for differentiation from the acquired form. The mere fact that the disease has already made its appearance at birth is of itself not of fundamental importance if there is no history of similar trouble in the family. I feel, therefore, that if the familial form (which, as a matter of fact, is usually, though not always, congenital) were opposed to the acquired form, the time of onset, as indicated by the term congenital, might well be disregarded. The possibility of an early acquisition of the disease is shown in the case reported by Beneck and Sabrazés.³⁹ With a negative family history, a suckling acquired the disease apparently from her wet-nurse, who, together with her two children, had a chronic hemolytic jaundice. Certain authors consider the two types identical. Hynek,⁴⁰ for instance, bases his opinion on two cases observed by him, the mother acquiring the disease after childbirth, whereas with her child it appeared congenitally. Plehn⁴¹ reports a case appearing congenitally in father and daughter, but not until the twenty-sixth year in the case of a son. Benjamin and Sluka⁴² observed three

³⁷ Ueber Hemolytischer Icterus und Seine Behandlung durch Splenectomie, *Verh. d. deut. Kong. f. inn. Med.*, 1913, xxx, 326.

³⁸ Ueber die Hemolytische Anämie, *Deut. Arch. klin. Med.*, 1912, cvi, 138; *Der Angeborene Hemolytische Icterus*, *Corresp. Schweiz. Aerzt.*, 1913, xliii, 689.

³⁹ Ictère Hemolytique Chronique, Avec Splénomégalie, *Gaz. Heb. Sci. Méd. de Bordeaux*, 1909, xxx, 469.

⁴⁰ Chronischer Icterus mit Milztumor ohne Bilirubinurie, *Casopis Lekaru, ceskych.*, 1906, p. 1029. (Ref. Schmidt's Jahrb., 1907, cxciv, 160.)

⁴¹ Familial Milz und Leber Vergrösserungen mit Anämie, und Gutartiger Verlauffung, *Deut. med. Woch.*, 1909, xxxv, 1749.

⁴² Chronische Acholurische Icterus mit und ohne Milztumor, *Berl. klin. Woch.*, 1907, xlv, 1065.

cases in one family, two appearing congenitally and one in adult life. Many of these could undoubtedly be harmonized if the time of onset was disregarded.

In favor of the identity of the two types it must be admitted that a series of cases could be selected in which many grades between the two types could be represented. It is obvious also that the familial type must at one time or another have originally been acquired. In such an event the difference in severity between the acquired and familial still holds. Thus both in Roth's⁴³ and Bychorski's⁴⁴ cases the disease in the parent who acquired it was severe, while in the children who inherited it, it was of the usual mild type. Such facts, however, would not indicate a fundamental difference in the nature of the two diseases.

In the small number of cases already accumulated, various atypicalities have been reported. Thus, Lommel's⁴⁵ and Claus and Kalberlah's⁴⁶ cases of the familial type, and Mosse's⁴⁷ and Tixier's⁴⁸ cases of the acquired type failed to show any change in resistance of the red cells (either washed or of the whole blood), though other evidences of increased blood destruction were present. In a few cases also a similar acholuric jaundice with splenomegaly has existed together with polycythemia instead of anemia. A slightly different form has also been described by Chauffard and Vincent,⁴⁹ Van den Bergh⁵⁰ and Roth,⁵¹ in which homolysins are present in the blood, which, so to speak, occupies a midway position between hemolytic jaundice and paroxysmal hemoglobinuria "a frigore." Gibert⁵² and his pupils have published numerous reports since 1900 on similar conditions under the name of "cholemie familiale." They have at least served to call attention to the fact that variations may be found in the amount of enlargement of the spleen and liver. It is questionable, however, if it is necessary, as they have frequently done, to consider each atypical form as a separate condition to be dignified with a separate name. As many of their cases were described before the various hematological methods above described had come into vogue, and are frequently reported in resumé, it is difficult

⁴³ Loc. cit.

⁴⁴ Zur Kasuistik der Heredofamiliären Splenomegalien, Wien. klin. Woch., 1911, xxiv, 1519.

⁴⁵ Ueber die Sogenannte Bantische Krankheit und den Hemolytischen Ikterus, Deut. Arch. f. klin. Med., 1912, cix, 174.

⁴⁶ Ueber Chronischen Ikterus, Berl. klin. Woch., 1906, xliii, 1471.

⁴⁷ Zur Lehre der Krankheiten mit Gesteigertem Hämolyse, Berl. klin. Woch., 1913, l, 684.

⁴⁸ Ictère d'origine Hemolytique, Resistance des Hematies Desplasmatisées Sensiblement Normale, Comp. Rendu de la Soc. de Biol., 1908, lxiv, 43.

⁴⁹ Hemoglobinurie Hemolysinique avec Ictère Polycholique Aigu, Semaine Méd., 1909, xxix, 601.

⁵⁰ Ictère Hemolytique avec Crises Hemoglobinuriques, Fragilité Globulaire, Rev. de Méd., 1911, xxxi, 63.

⁵¹ Zur Frage des "Ictère Hemolysinique" (Chauffard), Deut. Arch. klin. Méd., 1913, cx, 77.

⁵² Loc. cit.

to tell for sure whether or not they should be considered as belonging to the types under discussion. Their theory of hepatic origin, due to an infectious angiocholitis, was later abandoned by them in favor of Chauffard's idea that the primary change was in the blood.

All the symptoms of increased blood destruction may be present and yet icterus be absent. Thus, Chauffard describes a family in which the mother is a typical hemolytic icteric, while the eighteen-year-old son presents all the signs except the jaundice.

When the anemia is grave the blood may present a picture indistinguishable from pernicious anemia (v. Stejskal).⁵³ Chauffard considers that there is an icteric form of pernicious anemia which, when accompanied by diminished resistance and reticulated red cells, represents the least compensated form of hemolytic icterus. Widal and Weissenbach⁵⁴ have also reported a case of this type. In the usual Biermer type of pernicious anemia, icterus is absent and the resistance of the red cells increased.

Banti⁵⁵ has recently proposed the name hemolytic splenomegaly for a type of case which on analysis is indistinguishable from the acquired form of hemolytic jaundice. The two cases described by him (one an aplastic subvariety) both exhibit a chronic anemia, with long-standing splenomegaly, subicterus, diminished resistance of the red cells, increased number of reticulated cells, and urobilinuria. The beneficial effects of splenectomy, abolishing the anemia and changing the resistance to normal—in one case even changing an aplastic into a reacting bone marrow—lead him to ascribe a primary role in this disease to the spleen. It must be remembered, of course, that removal of the normal spleen indirectly causes an increase in resistance of the red cells. Banti claims never to have seen Widal's crises of deglobulization in these patients, and emphasizes the presence of a relative lymphocytosis; but this would hardly indicate a different disease. As to the choice of name, Banti's is open to the same objection as the other, namely, that splenomegaly may be absent in some cases (Le Gendre,⁵⁶ Pick,⁵⁷ Gilbert,⁵⁸ Benjamin and Sluka's third case, and Marchiafava and Nazzari⁵⁹) just as jaundice is in others. A name indicating increased blood destruction, such as hemolytic hypersplenism, without including individual features, would be less open to

⁵³ *Über Hemolytischen Icterus und über den Auftreten Hemolytischen Vorgänge bei diesem und bei Perniciöse Anämie*, Wien. klin. Woch., 1909, xxii, 661.

⁵⁴ *Anémie Pernicieuse Cryptogénétique avec Hemolysinhémie et Fragilité Globulaire Alternante*, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1913, xxix, 250.

⁵⁵ *La Splenomegalia Emolitica, Sperimentale*, 1912, lxvi, 91; *La Splenomegalia Emolitica Anemopoietica, Sperimentale*, 1913, lxvii, 323.

⁵⁶ *Deux observations d'Ictère Hemolytique l'un Congénitale l'un Acquis*, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxvii, 112.

⁵⁷ *Ueber hereditärischem Ikterus*, Wien. klin. Woch., 1903, xvi, 493.

⁵⁸ *Loc cit.*

⁵⁹ *Sugli Itteri Emolitici*, Bull. d. Reale Accad. di Roma, 1909, xxxv, 152.

objection; but in the meantime the name sanctioned by usage is preferable.

PATHOGENESIS. As I have already indicated in the discussion of the differentiation of the two types, an hepatic or luetic etiology has been largely discarded for the idiopathic primary types. There remain the two views, that the primary lesion is in the blood, a dystrophy of the red cells; or either primarily or indirectly in the spleen, an exaggerated hemolytic activity. Widal and his school, the extreme supporters of the former view, consider that the congenitally weak red-blood cells are destroyed in the circulation and their remains taken up by the spleen (causing a spodogenous tumor) and by the liver, kidney, and bone marrow (hence the excessive pigment found in these organs at autopsy). This view was supported by Vaquez,⁶⁰ von Stejskal, Benjamin and Sluka, Aschenheim⁶¹ and Weber and Dorner.⁶² The chief objection to it is that it completely ignores the great improvement following splenectomy. A primary increased hemolytic activity of the spleen as the source of the malady was first proposed by Minkowski and supported by von Krannhals and Chauffard. Its latest adherent, Banti, as I have previously stated, considers that the pathological spleen not only is spodogenous, but actively destroys increased numbers of cells and prepares others for destruction. Though based on incorrect and inadequate experimental evidence, this attractive combination of the splenogenous and hemocatonistic theories at present seems most plausible. Although it is not possible to demonstrate hemolysis by the normal spleen, we cannot exclude the possibility that that organ may in such diseased conditions, as Banti claims, take on increased hemolytic activity. Extracts from the spleens of Antonelli's⁶³ and Kahn's⁶⁴ cases, however, failed to show any hemolytic activity.

Whatever the source of the increased blood destruction may be, there results an increased amount of hemoglobin to be got rid of. The majority of authorities believe that it is changed by the liver into bile in excessive amounts, viscid and highly pigmented, which clog the bile capillaries, are resorbed into the blood, and thus cause a "pleichromic icterus." Recent investigations by Whipple,⁶⁵ however, show that bilirubin can be formed by the action of endothelium of bloodvessels entirely isolated from the hepatic circulation.

⁶⁰ Ictère chronique acholurique avec splénomégalie, *Bull. et. Mém. Soc. Méd. Hôp. Par.*, 1907, xxiv, 1184; *Sur l'Anatomie Pathologique de L'Ictère Hemolytique*, *Arch. des Mal. de Cœur.*, 1908, i, 609.

⁶¹ Ueber Familiären Hämolytischen Icterus, *Münch. med. Woch.*, 1910, lvii, 1282.

⁶² Four Cases of Congenital Acholuric So-called Hemolytic Jaundice in One Family, *Lancet*, 1910, i, 227. Acquired Chronic Acholuric Jaundice, *AMER. JOUR. MED. SCI.*, 1909, cxxxviii, 24.

⁶³ Intorno all'Effetti della Splenectomia su Ittero Emolitica Acquisita con Anemia a Tipo Perniciosa, *Polidlinico (Par. Med.)*, 1913, xx, 3.

⁶⁴ *Loc cit.*

⁶⁵ Icterus, *Jour. Exp. Med.*, 1913, xvii, 612.

If this be true a hematogenous icterus in the narrower sense can be accepted. That the jaundice is not due to gross obstruction is proved by the facts that such obstruction has never been found, that the stools are of normal color, and that the urine does not contain bilirubin.

It is interesting to note that in Banti's aplastic or anemopoietic case, splenectomy started the regenerating powers of the bone marrow as shown by the appearance of normoblasts in the circulating blood. This would indicate that with the spleen there was removed a toxin that had inhibited blood formation and would argue that the weakened red cells of hemolytic jaundice are due, not to hemocatatonic action of the spleen, but to an indirect injury to the bone marrow.

PATHOLOGY. Of the comparatively few cases that have come to autopsy or splenectomy a study of the morbid anatomy has not been very productive. I have collected eight autopsies and seven splenectomies, with the results shown in table on opposite page.

THERAPEUTICS. Views as to the treatment of these conditions have changed fundamentally in the past few years. Following Vaquez and Giroux's⁶⁶ case, in which death ensued two days after splenectomy, came Chauffard's dictum that hemolytic jaundice constituted a "Noli me tangere" for the surgeon. Various surgical attempts on the bile passages (Chauffard and Troisier;⁶⁷ Marchiafava and Nazzari; Widal, Abrami and Brulé); x-rays (Benjamin and Sluka); bone marrow feeding (Chauffard, Widal); cholagogues (Chauffard, Cavazza)⁶⁸ all proved unavailing. Only with a long-continued course of iron diet did Widal find some improvement. On account of the antihemolytic properties of arsenic (Gunn and Feltham)⁶⁹, cholesterin (Chauffard and Grigaut,⁷⁰ Parisot and Heully⁷¹), and calcium chloride (Iscovesco⁷²), these drugs have been tried, in some cases with improvement, apparently due to increasing the resistance of the red cells. No curative measure had been produced, however, when splenectomy was again tried in 1911, with very different results. In that year Micheli removed the spleen from a case of the acquired type, with the most striking improvement; the blood count which had been between 980,000 and 2,600,000 quickly rose to almost normal, the acholuric jaundice and urobiluria disappeared, the fragility of the red cells was lessened, and the patient within a few months was apparently

⁶⁶ Ictère chronique acholurique avec Splénomégalie, *Bull. et Mém. Soc. Méd. Hôp. de Paris*, 1907, xxiv, 1184.

⁶⁷ Des Rapports de Certaines Anémies Splénomégaliqes avec L'Ictère Hémolytique Congénitale, *Bull. et Mém. Soc. Méd. des Hôp. de Paris*, 1909, xxvii, 293.

⁶⁸ Gli Itteri Emolitici-Milano, 1911.

⁶⁹ The Antihemolytic Power of Arsenic, *British Med. Jour.*, 1911, i, 134.

⁷⁰ Le Taux de la cholestérinémie au cours des cardiopathies, *Comp. Rend. Soc. Biol.*, 1911, lxx, 108.

⁷¹ Le Traitement des Ictères Hémolytiques, *Semaine Méd.*, 1913, xxxiii, 85.

⁷² Les Lipoides du Sang. La Cholestérine, *Comp. Rend. Soc. Biol.*, 1908, lxiv, 404. See also *ibid.*, 1907, lxxiii, 744.

TABLE II.—PATHOLOGY OF HEMOLYTIC JAUNDICE.

Author.	Type.	Based on	Weight of spleen.	Capsule and trabeculae.	Pulp.	Sinus.	Malpighian follicles.	Pigment in spleen.	Phagocytes in spleen.	Pigment in liver.	Bone marrow.	Miscellaneous.
Minkowski	Familial.	Autopsy.	Gms. 675	Normal.	Congestion.	Congestion.	...	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Vaquez and Giroux	Familial.	Autopsy.	850	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	Normal.	Red.	
Gandy and Brul ⁷³	Familial.	Autopsy.	750	Normal.	Marked congestion.	Congestion.	Normal.	Slight increase.	Increase.	Normal.	Red.	
Marchalava	Familial.	Autopsy.	270	Thick.	...	...	Necrotic.	Increase.	...	Increase.	...	Spleen slightly fibrotic.
Oettinger ⁷⁴	Acquired.	Autopsy.	575	Normal.	Marked congestion.	Congestion.	Small.	Increase.	Increase.	Increase.	Red.	Much pigment in kidneys.
Micheli	Acquired.	Autopsy.	850	Thick.	Congestion.	Congestion.	No germ centres.	Increase.	Slight increase.	Normal.	Red.	Endothelial cells of spleen increased. Liver fibrotic.
Kahn 1	Familial.	Operation.	970	Normal.	Congestion.	Congestion.	Normal.	Increase.	...	...	...	Few pulp cells in spleen.
Kahn 2	Familial.	Operation.	1170	Thick.	Congestion.	Congestion.	Few.	Slight increase.	...	...	...	
Umber	Acquired.	Operation.	1300	Normal.	Congestion.	Congestion.	Pigmented and congested.	Increase.	Increase.	Increase.		
Antonelli	Acquired.	Operation.	1000	Normal.	Congestion.	Congestion.	Normal.	Increase.	Increase.	Increase.		
Fiori	Acquired.	Operation.	1000	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	Increase.		
Banti 1	Acquired.	Operation.	1580	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	Increase.		
Banti 2	Acquired.	Operation.	970	Normal.	Marked congestion.	Congestion.	Normal.	Increase.	Increase.	...	...	Endothelial cells of spleen necrotic.
Gaisböck	Acquired.	Autopsy.	?	Normal.	Not congested.	Not congested.	?	Increase.	Increase.	Increase.	Red.	Myeloblasts in liver and spleen.

⁷³ Gandy, C., and Brulé, M. Ictère Hemolytique Congénitale Autopsie, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1909, xxviii, 369.

⁷⁴ Oettinger, W. Sur un Cas d'Ictère d'Origine Hemolytique non Congénitale, Bull. et Mém. Soc. Méd. Hôp. de Paris, 1908, xxvi, 391.

cured. Similar beneficial results were obtained by Banti in his two cases of hemolytic splenomegaly, which I have taken to be identical with the acquired form of hemolytic jaundice. In the past two years splenectomy has been performed successfully in both acquired and familial types in cases reported by Antonelli, De Castello, Kahn, Lankhout,⁷⁵ Fiori⁷⁶ and Eppinger.⁷⁷ In no cases were there any bad results, and all showed a great improvement in symptoms, with specific evidence of lessened blood destruction. It is, of course, too early to know whether the improvement is but temporary or whether permanent cure has been effected.⁷⁸

With such gratifying results and the analogous hyperthyroidism in mind, it is not surprising that the procedure should be applied to related conditions such as hypertrophic cirrhosis and pernicious anemia. Eppinger⁷⁹ considers that the amount of hemolysis in a given case can be determined by the iodine count of the blood fat (normal 80 to 90) and the amount of urobilin in the feces (normal 0.12 to 0.15 gm. per day). He found both these increased not only in hemolytic jaundice, but also in pernicious anemia, hypertrophic cirrhosis, and catarrhal jaundice. As he and King had found experimentally that removal of the spleen caused a great drop in the iodine content, (*i. e.*, lessened hemolysis), he proposed splenectomy in this type of case also. His latest theory of the pathogenesis of pernicious anemia is more fanciful. Having found thickened walls in the arterioles of the spleen, he assumes that the blood seeks the path of less resistance through Weidenreich's open capillaries into the pulp, where they are destroyed. Splenectomy therefore becomes equivalent to tying off a ruptured bloodvessel. This theory has not yet received widespread acceptance.

Klemperer's⁸⁰ summary of ten cases shows that the operative risk in pernicious anemia is considerable, and if successfully passed, an improvement which is not fundamental is the most to be hoped for. It is noteworthy that he bases the procedure on the incorrect hypothesis that splenectomy normally causes an increase in the number of red cells. Huber,⁸¹ De Castello⁸² and Mosse have also found im-

⁷⁵ Hemolytische Splenomegalia, *Nederl. Tijds. d. Geneesk.*, 1913, lvii, 1153.

⁷⁶ Un caso di Splenomegalica Emolitica Trattata colla Splenectomia, *Sperimentale*, 1913, lxxvii, 189.

⁷⁷ Zur Pathologie der Milzfunktion, *Berl. klin. Woch.*, 1913, I, 1509 and 2409.

⁷⁸ Since the above was written, the patient to whom I have previously referred has also successfully undergone splenectomy, with great improvement of clinical symptoms and return of blood picture almost to normal. His case with metabolic studies before and after splenectomy will shortly be reported by Pearce, Pepper, and Goldschmidt. The results of splenectomy in hemolytic jaundice have very recently been collected by Elliott and Kanavel (*Surg., Gyn. and Obstet.*, 1915, xxi, 21). Of 48 cases splenectomized, 2 have died, and in the 46 "cures," practically all symptoms of the disease have disappeared.

⁷⁹ *Loc. cit.*

⁸⁰ In welcher Krankheit Kommt die operative Entfernung der Milz in Frage? *Ther. d. Gegenwart*, 1914, lv, 1.

⁸¹ Ueber die Blut Veränderungen bei Icterus Hemolyticus, *Berl. klin. Woch.*, 1913, I, 681 and 2179.

⁸² Ueber den Einfluss der Milzextirpation auf der Perniciöse Anämie, *Deut. med. Woch.*, 1914, xl, 639.

provement after splenectomy in an icteric type of pernicious anemia. It is interesting that in Huber's case the blood cells from the splenic vein showed no decrease in resistance. As all three patients had icterus, urobilinuria, fragility of corpuscles, and splenomegaly it is probable that these cases really belong to the class of hemolytic jaundice.

One might say in summarizing that splenectomy should be considered in all those diseases where there is evidence of increased blood destruction and that in early Banti's disease and hemolytic jaundice at least the results of splenectomy have been excellent. All such procedures, however, should be entered upon most conservatively as long as so much of the physiology of the spleen remains unknown. Though its removal is known to be compatible with life, it may yet prove to have such important detoxicating relations to infection or to digestion, that splenectomy should only be practised after most careful study and to relieve the most serious conditions.⁸³

CULTURAL AND VACCINE RESULTS IN A CASE OF HODGKIN'S DISEASE.

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IN the number of the *Archives of Internal Medicine*, for August, 1913, Bunting and Yates report six cases of Hodgkin's disease, from the lymphatic glands of which they have isolated a diphtheroid organism considered by them as identical with the one described by Fraenkel and Much.¹ In 1900 the last-named authors were able to extract Gram-positive, non-acid-fast, diphtheroid bacilli from the sediment of the lymph glands which had been previously treated with antiformin, to which preparation the organism was resistant.

Negri and Miermet² were the first to report successful cultivation of this organism, isolation of which was brought about on Bordet's medium (blood-glycerin-potato-agar).

Billings and Rosenow³ have isolated the same organism from eighteen cases of Hodgkin's disease, the glands of which were

⁸³ Since the above was written, numerous reports of splenectomy for pernicious anemia have appeared. Though the patient's general condition was improved temporarily in many cases, in no case has definite cure resulted, or the blood picture of pernicious anemia been fundamentally changed.

¹ *Ztschr. f. Hyg.*, 1910, xvii, 189.

² *Centralblatt f. Bak.*, 1913, lxxviii, 292.

³ *Jour. Amer. Med. Assoc.*, December, 1913.